

INTERNATIONAL SEARCH REPORT

Application No
PCT/GB2005/000007

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/62 A61K47/48 C07K14/54 C07K16/30 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, BIOSIS, CANCERLIT, DISSERTATION ABS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HALIN CORNELIA ET AL: "Synergistic therapeutic effects of a tumor targeting antibody fragment, fused to interleukin 12 and to tumor necrosis factor alpha." CANCER RESEARCH, vol. 63, no. 12, 15 June 2003 (2003-06-15), pages 3202-3210, XP002342601 ISSN: 0008-5472	1-33
X	abstract figures page 3204, right-hand column - page 3207, right-hand column ----- -/--	34, 43-50



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

29 August 2005

Date of mailing of the international search report

12/09/2005

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	THORPE P E ET AL: "The First International Conference on Vascular Targeting: Meeting overview" CANCER RESEARCH 01 MAR 2003 UNITED STATES, vol. 63, no. 5, 1 March 2003 (2003-03-01), pages 1144-1147, XP002342602 ISSN: 0008-5472	1-33
X	page 1145, left-hand column	34, 43-50
X	----- HALIN C ET AL: "Enhancement of the antitumor activity of interleukin-12 by targeted delivery to neovasculature" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 20, no. 3, March 2002 (2002-03), pages 264-269, XP002256784 ISSN: 1087-0156	1-33
X	the whole document	34, 43-50
X	----- WO 03/093478 A (MOLMED SPA; CORTI, ANGELO; CURNIS, FLAVIO) 13 November 2003 (2003-11-13) page 5, line 32 - line 33 page 26 claims	1-34, 43-50
X	----- HUANG X ET AL: "TUMOR INFARCTION IN MICE BY ANTIBODY-DIRECTED TARGETING OF TISSUE FACTOR TO TUMOR VASCULATURE" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 275, 24 January 1997 (1997-01-24), pages 547-550, XP002071588 ISSN: 0036-8075 the whole document	1-34, 43-50
Y	----- VAN VLIET A I ET AL: "Distribution of fibronectin isoforms in human renal disease" JOURNAL OF PATHOLOGY 2001 UNITED KINGDOM, vol. 193, no. 2, 2001, pages 256-262, XP002342603 ISSN: 0022-3417 abstract page 257, left-hand column, last paragraph - right-hand column, paragraph 1 page 258; figure 1 page 260; table 2	1-34, 43-50
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	VITI F ET AL: "Increased binding affinity and valence of recombinant antibody fragments lead to improved targeting of tumoral angiogenesis" CANCER RESEARCH 15 JAN 1999 UNITED STATES, vol. 59, no. 2, 15 January 1999 (1999-01-15), pages 347-352, XP002124782 ISSN: 0008-5472 abstract page 348 - page 350	1-34, 43-50
Y	----- CARNEMOLLA B ET AL: "A tumor-associated fibronectin isoform generated by alternative splicing of messenger RNA precursors" JOURNAL OF CELL BIOLOGY 1989 UNITED STATES, vol. 108, no. 3, 1989, pages 1139-1148, XP002342604 ISSN: 0021-9525 abstract page 1140, right-hand column, paragraph RESULTS - page 1144, right-hand column figure 5 table III	1-34, 43-50
Y	----- ZHU Z ET AL: "INHIBITION OF TUMOR GROWTH AND METASTASIS BY TARGETING TUMOR-ASSOCIATED ANGIOGENESIS WITH ANTAGONISTS TO THE RECEPTORS OF VASCULAR ENDOTHELIAL GROWTH FACTOR" INVESTIGATIONAL NEW DRUGS, MARTINUS NIJHOFF PUBLISHERS, BOSTON, US, vol. 17, no. 3, 1999, pages 195-212, XP000940444 ISSN: 0167-6997 page 202, right-hand column	1-34, 43-50
Y	----- PENG L S ET AL: "Mechanism of antitumor activity of a single-chain interleukin-12 IgG3 antibody fusion protein (mscIL-12.her2.IgG3)" JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, vol. 21, no. 9, 2001, pages 709-720, XP002342605 ISSN: 1079-9907 abstract page 712 - page 715; figures page 715, left-hand column, last paragraph - right-hand column, paragraph 2 ----- -/--	1-34, 43-50

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LADELL KRISTIN ET AL: "A combination of plasmid DNAs encoding murine fetal liver kinase 1 extracellular domain, murine interleukin-12, and murine interferon-gamma inducible protein-10 leads to tumor regression and survival in melanoma-bearing mice." JOURNAL OF MOLECULAR MEDICINE (BERLIN), vol. 81, no. 4, April 2003 (2003-04), pages 271-278, XP002342606 ISSN: 0946-2716 abstract figures	1-34, 43-50
Y	DICKERSON ERIN B ET AL: "Development of an IL-12 fusion protein for molecular targeting of tumor vasculature" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, no. 41, March 2000 (2000-03), page 798, ABSTRACT NO. 5074, XP002342607 & 91ST ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH.; SAN FRANCISCO, CALIFORNIA, USA; APRIL 01-05, 2000 ISSN: 0197-016X the whole document	1-34, 43-50
Y	WO 99/29732 A (LEXIGEN PHARMACEUTICALS CORPORATION) 17 June 1999 (1999-06-17) cited in the application	1-34, 43-50
X	examples 1,4-7 claims	35-42
Y	WO 02/02143 A (LEXIGEN PHARMACEUTICALS CORP) 10 January 2002 (2002-01-10) examples	1-34, 43-50
Y	MAJEWSKI S ET AL: "INTERLEUKIN-12 INHIBITS ANGIOGENESIS INDUCED BY HUMAN TUMOR CELL LINES IN VIVO" JOURNAL OF INVESTIGATIVE DERMATOLOGY, NEW YORK, NY, US, vol. 106, no. 5, 1996, pages 1114-1118, XP000949299 ISSN: 0022-202X abstract page 1116 - page 1117	1-34, 43-50

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 47 is directed to a method of treatment of the human/animal body, a search has been carried out, based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 51-52
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claim 47 is directed to a method of treatment of the human/animal body, a search has been carried out, based on the alleged effects of the compound/composition.

Continuation of Box II.2

Claims Nos.: 51-52

Claims 51-52 do not contain technical features, and can therefore not be searched.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-34, 43-50

Compound containing of a portion targeting oncofoetal fibronectin and IL-12 as effector portion, pharmaceutical composition containing it, and its use in the treatment of cancer, according to these claims.

2. claims: 35-39

Nucleic acid encoding the fusion protein of anti-oncofoetal fibronectin and IL-12, or encoding part of it.

3. claims: 40-42

Expression vector as claimed, host cell as claimed, and their use in the method of making a compound as claimed

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on patent family members

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03093478	A	13-11-2003	AU 2003228057 A1	17-11-2003
			CA 2462879 A1	13-11-2003
			EP 1499730 A1	26-01-2005
			WO 03093478 A1	13-11-2003
			US 2005033026 A1	10-02-2005
WO 9929732	A	17-06-1999	AT 267215 T	15-06-2004
			AU 763719 B2	31-07-2003
			AU 1716099 A	28-06-1999
			CA 2312188 A1	17-06-1999
			DE 69824039 D1	24-06-2004
			DE 69824039 T2	18-08-2005
			DK 1037927 T3	06-09-2004
			EP 1489100 A2	22-12-2004
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			ES 2221717 T3	01-01-2005
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			WO 9929732 A2	17-06-1999
WO 0202143	A	10-01-2002	AU 7172901 A	14-01-2002
			BR 0112111 A	06-05-2003
			CA 2412845 A1	10-01-2002
			CN 1529619 A	15-09-2004
			CZ 20030214 A3	13-08-2003
			EP 1294401 A2	26-03-2003
			HU 0300868 A2	28-07-2003
			JP 2004501981 T	22-01-2004
			MX PA02012734 A	25-04-2003
			NO 20026245 A	26-02-2003
			PL 358582 A1	09-08-2004
			SK 982003 A3	04-05-2004
			WO 0202143 A2	10-01-2002
			US 2003049227 A1	13-03-2003
			ZA 200300759 A	28-04-2004